

Amendments to the Specification:

On page 2, please amend the paragraph starting on line 8 as follows:

-- Another chelidonine derivative is ~~ekraine~~ ukraine which, as a trimeric compound from celandine alkaloids, is used together with thiophosphoric triazide in cancer therapy. As has been demonstrated, antitumor effectiveness of ~~ekraine~~ ukraine has been detected in cell cultures and in animal experiments. Furthermore, some disclosures reveal that ~~ekraine~~ ukraine has a therapeutic effect in humans in cases of prostate carcinomas, colorectal carcinomas and breast cancer. To date, however, it has not been possible to determine which active substances included in different lots of ~~ekraine~~ ukraine are responsible for the above-described antitumor effect. For the time being, none of the agents being used has been officially approved in the EU member states. --

On page 2, please amend the paragraph starting on line 32 as follows:

-- The invention solves the above problem by providing new chelidonine derivatives having an antitumoral effect, selected from the group comprising chelidonine acetate, chelidonyl trifluoroacetate, ~~chelidonine~~ chelidonyl trichloromethyl carbonate, ~~chelidonine~~ chelidonyl methyl succinate, chelidonyl ethyl oxalate, N-(3-trifluoromethylphenyl)chelidonylurethane, phenylalanine chelidonyl ester, proline chelidonyl ester and/or alanine chelidonyl ester.---

On page 4, please amend the paragraph starting on line 22 as follows:

-- For example, injections (intramuscular or subcutaneous or into blood vessels) are envisaged as a route of therapeutic administration of the compounds of the invention, e.g. encapsulated or carrier-bound compounds of the invention, although supply in the form of an aerosol, via catheters or surgical tubes is also applicable. Other preferred routes include suspensions, tablets, capsules and the like for oral administration, commercially available nebulizers for liquid formulations and inhalation of lyophilized or aerolyzed compounds and suppositories for rectal or vaginal administration. Liquid formulations can be solutions, syrups, fluid mixtures, suspensions, emulsions, sterile drug forms (sterile ampoules, septum vials, infusions, lyophilizates) and/or lotions. The suitability of the selected parameters, e.g. dosage, regimen, selection of adjuvants and the like can be determined by taking serum aliquots from the patient, i.e. human or animal, and testing during the course of the applications. Alternatively or concomitantly, the amount of T

*Second Preliminary Amendment
National Stage of PCT/DE05/01181*

cells or other cells of the immune system can be determined in a conventional manner so as to obtain an overall survey of the patient's immunologic constitution. In addition, the clinical condition of the patient can be observed for the desired effect. In particular, growth and metastasizing of tumors can be determined. As tumors can be associated with other diseases, e.g. infections, additional co-monitoring of the latter is also possible. --

On page 8, please amend the paragraph starting on line 18 as follows:

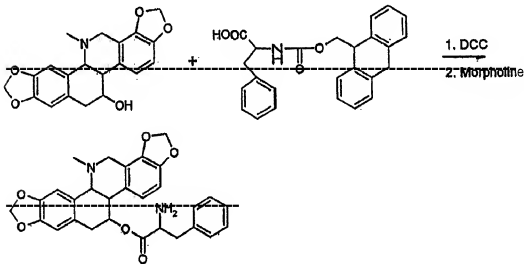
-- Furthermore, the salts can be free of carboxyl groups and derived from inorganic bases such as sodium, potassium, ammonium, calcium or iron hydroxides, or from organic bases such as isopropylamine, trimethylamine, 2-ethylaminoethanol, histidine and others. Examples of liquid carriers are sterile aqueous solutions including no further materials or active ingredients, e.g. water, or those comprising a buffer such as sodium phosphate with a physiological pH or a physiological salt solution or both, such as phosphate-buffered sodium chloride solution. Other liquid carriers may comprise more than just one buffer salt, e.g. sodium and potassium chlorides, dextrose, propylene glycol, polyethylene glycol, or others. Liquid compositions of the pharmaceutical agents may additionally comprise a liquid phase, with water being excluded, however. Examples of such additional liquid phases are glycerol, vegetable oils, organic esters or water-oil emulsions. The pharmaceutical composition or pharmaceutical agent typically includes a content of at least 0.1 wt.-% of compounds according to the invention, relative to the overall pharmaceutical composition. The respective dose or dosage range for administering the pharmaceutical agent according to the invention is sufficiently high or wide in order to achieve the desired prophylactic or therapeutic effect of forming neutralizing antibodies. In this context, the dose should not be selected in such a way that undesirable side effects would dominate. In general, the dose will vary with the patient's age, constitution, sex and, of course, depending on the severity of the disease. The individual dose can be adjusted both with reference to the primary disease and with reference to the occurrence of additional complications. Using well-known means and methods, the exact dose can be determined by a person skilled in the art, e.g. by determining the tumor growth as a function of dosage or as a function of the application regime or pharmaceutical carrier and the like. Depending on the patient, the dose can be selected individually. For example, a dose of pharmaceutical agent just tolerated by a patient can be such that the range thereof in plasma or locally in particular organs is from 0.1 to

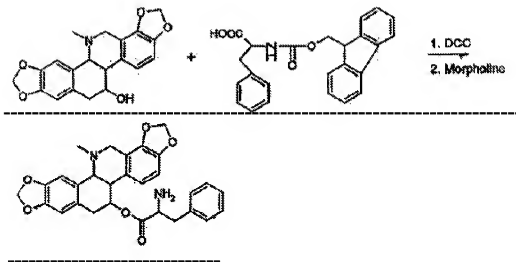
10,000 μM , preferably between 1 and 100 μM . Alternatively, the dose can be calculated relative to the body weight of the patient. In this event, a typical dose of pharmaceutical agent would have to be adjusted e.g. in a range between 0.1 μg and 100 μg per kg body weight, preferably between 1 and 50 $\mu\text{g}/\text{kg}$. Furthermore, however, it is also possible to determine the dose on the basis of particular organs rather than the whole patient. For example, this would be the case when placing the pharmaceutical agent according to the invention, e.g. in a biopolymer incorporated in the respective patient, near specific organs by means of surgery. Several biopolymers capable of liberating peptides or recombinant proteins in a desirable manner are known to those skilled in the art. For example, such a gel may include 1 to 1000 μg of ~~amine acid sequences~~ the compositions of the invention, e.g. peptides or recombinant proteins, or of pharmaceutical agent per ml gel composition, preferably between 5 and 500 $\mu\text{g}/\text{ml}$, and more preferably between 10 and 100 mg/ml . In this event, the therapeutic agent is administered as a solid, gel-like or liquid composition. –

On page 30, please amend the paragraph starting on line 1 as follows:

-- Reaction:

Reaction of chelidonium monohydrate (Fluka Ch:425201/1) with N-(9-fluorenylmethyloxycarbonyl)-L-phenylalanine (Aldrich)





Chelidonium monohydrate: m.w. = 371.39 g/mol

N-(9-Fluorenylmethyloxycarbonyl)-L-phenylalanine:

m.w. = 387.44 g/mol

Dicyclohexylcarbodiimide (DCC): m.w. = 206.33 g/mol

Phenylalanine chelidonyl ester: m.w. = 500.52 g/mol, C₂₉H₂₈N₂O₆

Yield: 41.1% (113.9 mg) --

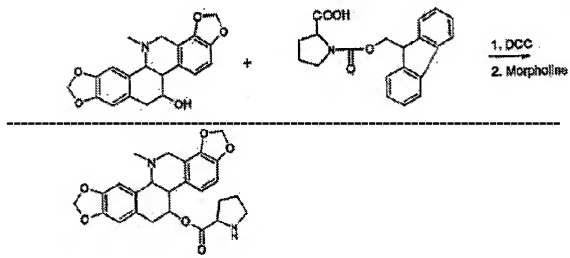
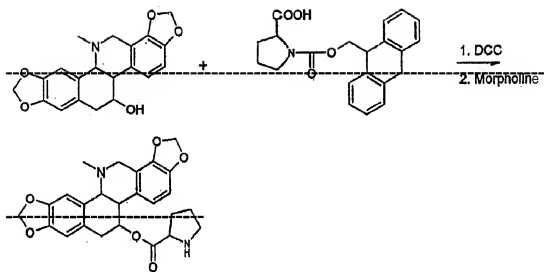
On page 31, please amend line 1 as follows:

-- 6. Preparation of ~~proline~~ chelidonyl prolyl ester --

On page 31, please amend the paragraph starting on line 10 as follows:

-- Reaction:

Reaction of chelidonium monohydrate (Fluka Ch:425201/1) with N-(9-fluorenylmethyloxycarbonyl)-L-proline (Aldrich)



Chelidonine monohydrate: m.w. = 371.39 g/mol

N-(9-Fluorenylmethoxycarbonyl)-L-proline:

m.w. = 337.38 g/mol

Dicyclohexylcarbodiimide (DCC): m.w. = 206.33 g/mol

Proline chelidonyl ester: m.w. = 450.47 g/mol, C₂₅H₂₆N₂O₆

Yield: 36.3 (101.3 mg)₂ --

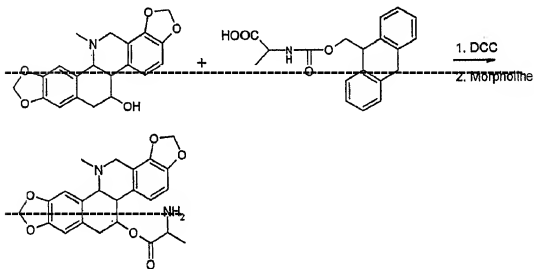
On page 32, please amend the paragraph starting on line 1 as follows:

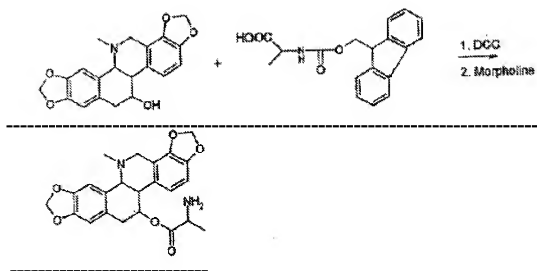
-- The preparation of ~~proline~~ chelidonyl prolyl ester (S10) is shown with reference to the IR and mass spectra (Figs. 7 and 8).---

On page 32, please amend the paragraph starting on line 10 as follows:

-- Reaction:

Reaction of chelidonine monohydrate (Fluka Ch:425201/1) with N-(9-fluorenylmethoxycarbonyl)-L-alanine (Aldrich)





Chelidonium monohydrate: m.w. = 371.39 g/mol

N-(9-Fluorenylmethoxycarbonyl)-L-alanine: m.w. = 311.32 g/mol

Dicyclohexylcarbodiimide (DCC): m.w. = 206.33 g/mol

Alanine chelidonyl ester: m.w. = 424.43 g/mol, $C_{23}H_{24}N_2O_6$

Yield: 33.5% (101.0 mg) --